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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1636	12

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,454	UHLER, MICHAEL D.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *1-33 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election of Group III (Claims 34-37) with traverse in Paper No. 11 is acknowledged. Examiner includes inadvertently claim 37 in Group III, even though it is already included in the invention of Group I. Claim 37 is more appropriately to be grouped together with the claims of Group I, drawn to a method of transfecting a cell with a transfection complex immobilized on a surface of the present invention, rather than a method of identifying a ligand of a receptor protein.

With respect to the traverse, the response argues that the examiner has not met his burden of establishing that examining the claims of the three groups in a single application will create a serious burden on the PTO. The response argues that claims 14-24 of Group II are misclassified under class 436, subclass 518, and that they should be more appropriately classified under class 435. Applicant's response also argues that claims 34-36 of Group III are misclassified under class 435, subclass 4, entitled "Measuring or testing process involving enzymes or microorganisms; composition or test strip therefore; processes of forming such composition or test strip," whereas the claims are directed to a method of identifying a ligand of a receptor which method includes a transfection complex and a cell. Applicant's response further argues that the Examiner does not provide arguments showing separate inventive efforts by inventors, and that Groups I-III share the common element of a transfection complex comprising nucleic acid and first and second complexing agents. Lastly, Applicant's response argues that a different field of search has not been demonstrated for the different groups of inventions, and that considerable overlap is likely in the search for the claims

in Groups I to III. Applicant's arguments are respectfully found to be unpersuasive for the following reasons.

Firstly, Applicant is correct in pointing out that the claims of Group II should be more appropriately classified under class 435, rather than under class 436. More specifically, the claims of Group II should be classified under class 435, subclass 395 or 402 (solid support and method of culturing cells on said solid support). Due to the breadth of the claims, they can also be classified under class 424, subclasses 422 and 423 (implant or insert), for examples. This is because Applicant is clearly contemplating immobilizing a transfection complex on a surface, such as cellulose acetate membranes, to be implanted into solid tumors in whole organisms (see specification on page 70, first full paragraph). It should also be noted that a transfection complex immobilized on a surface is also utilized for screening purposes in a cell culture.

Secondly, claims 34-36 of Group III drawn to a method of identifying a ligand of a receptor protein are properly classified under class 435, subclass 4, which includes subclass 6 (involving nucleic acid). This is because a method of identifying a ligand of Group III is a testing process for identifying a ligand of a receptor protein, and it should be further noted that a receptor protein is also an enzyme (e.g., receptor kinases).

Thirdly, the inventions of Groups I-III are distinct each from the others as they are drawn to methods having different starting materials, method steps, desired end-results and therefore they require different technical considerations for achieving the end-results. For examples, the invention in Group I is drawn to methods of transfecting a cell comprising contacting the cell with a transfection complex immobilized on a surface;

whereas the invention of Group II is simply directed to a method for immobilizing nucleic acid to a surface without requiring any cell or any contacting or transfecting step; the invention of Group III is drawn specifically to a method of identifying a ligand of a receptor protein involving different starting materials from those of the inventions of Groups I-II (e.g., the transfection complex comprises first and second nucleic acids wherein said first nucleic acid encodes a receptor and said second nucleic acid encodes a protein, wherein said first and second nucleic acid are present in at least one expression vector. Additionally, the transfection complex of Group I is not required to form an array as it is in the method of Group II.

Fourthly, the search for each of the above inventions is not exclusively based on its classification in a Patent database, but also on other non-patent literature search databases.

Accordingly, because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, and separate search requirements, it would be unduly burdensome for the examiner to search and/or consider the patentability of all the inventions in a single application. Therefore, restriction for examination purposes as indicated is proper. This requirement is made **FINAL**.

Therefore, claims 1-33 and 37 are withdrawn from further consideration because they are drawn to non-elected inventions.

Claims 34-36 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method of identifying a ligand of a receptor protein comprising:

a) providing:

1) a transfection complex immobilized on a surface, said complex comprising first and second nucleic acids and first and second complexing agents, said first nucleic acid encoding the receptor protein and said second nucleic acid encoding a selective marker operably linked to a cyclic AMP responsive promoter, wherein said first and second nucleic acid are present in at least one expression vector, and said first complexing agent comprising a candidate ligand for the receptor protein, and said second complexing agent comprising a DNA binding molecule, and

2) a cell;

b) contacting the cell with said complex under conditions such that the cell is co-transfected with the nucleic acids and the nucleic acids are expressed; and

c) detecting expression of the selective marker, wherein an enhanced expression of said selective marker indicates the presence of a ligand-receptor

protein binding pair, and wherein the receptor protein is encoded by said first nucleic acid;

does not reasonably provide enablement for a method of identifying a ligand of a receptor protein using any second nucleic acid encoding any protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

The claims are drawn to a method of identifying a ligand for a receptor comprising: a) providing: i) a transfection complex immobilized on a surface, said complex comprising first and second nucleic acids and first and second complexing agents, said first nucleic acid encoding a receptor and said second nucleic acid encoding a protein, wherein said first and second nucleic acid are present in at least one expression vector, and said first complexing agent comprising a ligand for a receptor, and said second complexing agent comprising a DNA binding molecule, and ii) a cell; and b) contacting the cell with said complex under conditions such that the cell is co-transfected with the nucleic acids and the nucleic acids are expressed; and c)

detecting the presence of a ligand-receptor binding pair, wherein the receptor protein is encoded by said first nucleic acid; the same method wherein said receptor protein is selected from the group consisting of G-protein coupled receptors and receptor kinases or wherein the immobilized nucleic acid form an array.

The instant specification is not enabled for such a broadly claimed invention for the following reasons.

(a) The breadth of the claims. The instant claims encompass a method of identifying a ligand for a receptor protein using a transfection complex immobilized on a surface, wherein the transfection complex contains any second nucleic acid encoding any protein.

(b) The state and the unpredictability of the art. At the effective filing date of the present application, activation of a receptor protein (e.g., G-protein coupled receptors or receptor kinases) by a ligand results in a complex cascade of signal transduction events, involving many signaling factors, and that that they are also variable depending on cell types being activated, as well as the nature of the ligand. Additionally, the physiological art is recognized as unpredictable (MPEP 2164.03).

(c) The amount of direction or guidance presented. Apart from the disclosure utilizing a cyclic AMP responsive promoter driving the expression of a destabilized green fluorescent protein (pCRE-d2EGFP) to monitor the activation of a membrane receptor by a specific ligand in a surface transfection and expression procedure (STEP) of the present invention (see example 15 and Fig. 3), the instant specification fails to provide sufficient guidance for a skilled artisan on how to use any second nucleic acid

encoding any protein in an immobilized transfection complex to detect the presence of a ligand-receptor binding pair in the method as claimed. For example, what other promoters and/or what other non-selective markers (including luminescence or flurorescence) that one can use to monitor the activation and therefore detecting the presence of a specific ligand-receptor binding pair in the method as claimed. Particularly, it is well known that the signaling cascade of any receptor protein for any given cell type is complex and it involves many interacting signaling molecules. Given the lack of sufficient guidance provided by the present disclosure, it would have required undue experimentation for a skilled artisan to make and use the method as claimed.

As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issues discussed above, the unpredictability of the physiological art, and the breadth of the instant claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 34 and its dependent claims, it is unclear what is encompassed by the phrase "detecting the presence of a ligand-receptor binding pair". Does Applicant mean the physical presence of a ligand-receptor binding pair being detected or the effects resulting from the interaction between a ligand-receptor binding pair being detected? Which ones? Additionally, there is no clear linkage between step (b) in which the cell is co-transfected with the nucleic acids and the nucleic acids expressed with step (c) for detecting the presence of a ligand-receptor binding pair. The metes and bounds of the claims are not clearly determined. Clarification is requested.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 34-36 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 34-36 of copending Application No. 10/002,802. This

is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gerald Leffers, Jr., Ph.D., may be reached at (703) 305-6232, or SPE, Remy Yucel, Ph.D., at (703) 305-1998.

Quang Nguyen, Ph.D.

GERRY LEFFERS
PRIMARY EXAMINER